The need for Interoperable Data to Support a Rapid Learning System for Cancer Care and Outcomes Analyses

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A Day In The Life…

Of a Pharmaceutical Outcomes Researcher

Pfizer Oncology

What Type of Questions Do I Ask?

- How do patients with a specific genotype or tumor-specific mutation fare on current standard of care therapy vs. patients without this biomarker?
  - Is there greater unmet medical need?
  - What is the historical survival pattern in these groups?
  - What is the potential magnitude of benefit of drugs targeted to this biomarker?
- How do side effect profiles of different drug regimens compare in actual clinical practice?
  - As used in a more heterogenous patient population
- What are major reasons of discontinuation or sub-optimal dosing of therapy?
  - What affects adherence to therapy?
- What is the patient-reported experience with drug regimens?
  - What is meaningful to the patient?
  - What supportive care and educational materials would help patients?

What Type of Data Do I Need?

Real-world practice data

- **Biomarker-linked clinical outcomes**
  - Available tissue specimens or available test results
  - Linkable to detailed medical records
- **Annotated, oncology-specific, medical records**
  - To capture dose reduction, delay, discontinuation and reasons thereof
- **Longitudinal, patient-reported outcomes**
  - From adequate, representative patient samples
- **Detailed personal, clinical, and pathology data**
  - e.g. exposure status (smoking), PS, stage, grade, histology

What Data are Available To Me Today?

- Administrative claims (billing) data
  - Large, managed care data sets
- Public use datasets
  - SEER, SEER-Medicare
- Institution-specific databases
  - NCCN Outcomes Databases
- Chart review
- EHR

A Fictitious Example from the “Real-World”

- A pharmaceutical company wants to look at adherence to its oral small molecule inhibitor (bestinib) compared to 2 of its competitors (greatinib and goodinib)
- All 3 drugs are labeled for use in the adjuvant setting for a particular tumor type
- All 3 drugs are in a similar class according to MOA
- An outcomes researcher on the bestinib team proposes to use claims data from a large, nationally representative payer to compare adherence to these 3 drugs

Results

Adherence Rate (6 months)	Drug Cohort		
	Bestinib (N = 1,698)	Greatinib (N = 1,953)	Goodinib (N = 1,837)
Adherence < 80%	8.8%	16.5%	19.4%
Adherence ≥ 80%	91.2%	83.5%	80.6%
Mean Adherence	95.4%	89.0%	83.8%

But…

Drug	Labeled Indication 1	Labeled Indication 2
Bestinib	Adjuvant treatment	
Greatinib	Adjuvant treatment after prior therapy	1st-line metastatic
Goodinib	Adjuvant treatment after prior therapy	2nd-line metastatic & Compendia-listed for 1st line metastatic

Adjuvant or Metastatic?

	Drug Cohort		
	Bestinib	Greatinib	Goodinib
Metastatic Cancer	0.3%	0.5%	0.5%
Bone Scans	16.7%	36.0%	51.4%
Chemotherapy Treatments	11.7%	29.3%	44.5%
CT Scans	29.7%	50.9%	67.4%
MRI Procedures	21.3%	31.8%	40.3%
Other metastatic site	3.7%	13.6%	28.0%

Results, Revisited

Adherence Rate (6 months)	Drug Cohort		
	Bestinib (N = 1,698)	Greatinib (N = 1,953)	Goodinib (N = 1,837)
Adherence < 80%	8.8%	16.5%	19.4%
Adherence ≥ 80%	91.2%	83.5%	80.6%
Mean Adherence	95.4% ~4% metastatic (Sick)	89.0% ~14% metastatic (Sicker)	83.8% ~27% metastatic (Sickest)

Conclusions?

Several things can explain non-adherence:

- Sicker patients (adjuvant vs. metastatic) may have lower adherence
- Disease progression or recurrence warrants change in therapy
- Side effects or adverse events leading to discontinuation
- Stable disease – may be able to take a break from therapy
- Planned “drug holidays” for life events
- Planned sequencing of therapy
- Off-label use

Limitations of Oncology Data Today

What's Missing?

- Adjuvant vs. metastatic (1st, 2nd, 3rd line +) treatment settings
- Stage, grade, histology, gene mutation status (biomarkers)
- Sites of metastatic spread
- Performance status
- History of prior neo-adjuvant therapy, surgery, radiation, adjuvant therapy or other lines of chemotherapy

What's Hard to Measure?

- Disease progression, recurrence, and survival
- Discontinuation of therapy due to AE's, progression, or stable disease
- Dose reductions and drug holidays

In many cases, chart review

is still needed!

Available Oncology Data

Data Source	Pro's 	Con's 
Claims Data	**Can estimate costs linked to treatment and medical procedures**	**Errors, missing clinical information, e.g. stage, histology, reasons for discontinuation, no biomarker data**
SEER, SEER-Medicare	**SEER: Has stage, histology, and survival; SEER-Medicare: Can estimate costs linked to tx**	**Long lag time means current tx data not available; Hard to determine recurrence/relapse; Data on oral agents**
NCCN Outcomes Databases	**Incident case cohorts, complete medical and tx history; complete outcomes data capture (survival)**	**Non-generalizable to community oncology setting; Databases are slow & expensive to build and to accumulate large sample sizes**
Chart Review	**Currently, most complete source of treatment data**	**Labor-intensive, missing data elements (pathology reports, lab & radiology data), need to manually link datasets (e.g. medical & cost data)**
EMR	**Easily searchable, unique data can be linked**	**Missing data (pathology) – Need Oncology-Specific data dictionary!**

Integrative Research Collaborations – Duke/Pfizer

- **CRC**
  - Chart review on tx patterns, outcomes
- **Breast**
  - e-PRO data collection
- **Melanoma**
  - Duke melanoma database
  - Tumor registry data
- **Pathfinders**
  - Holistic supportive care program linking clinical, e-PRO, and cost data
- **RCC (planned)**
  - e-PRO, chart review, clinical and economic data linkage
- **Lung (concept)**
  - Prospective cohort linking community and academic center data
  - Tissue specimens for biomarker-linked outcomes analyses

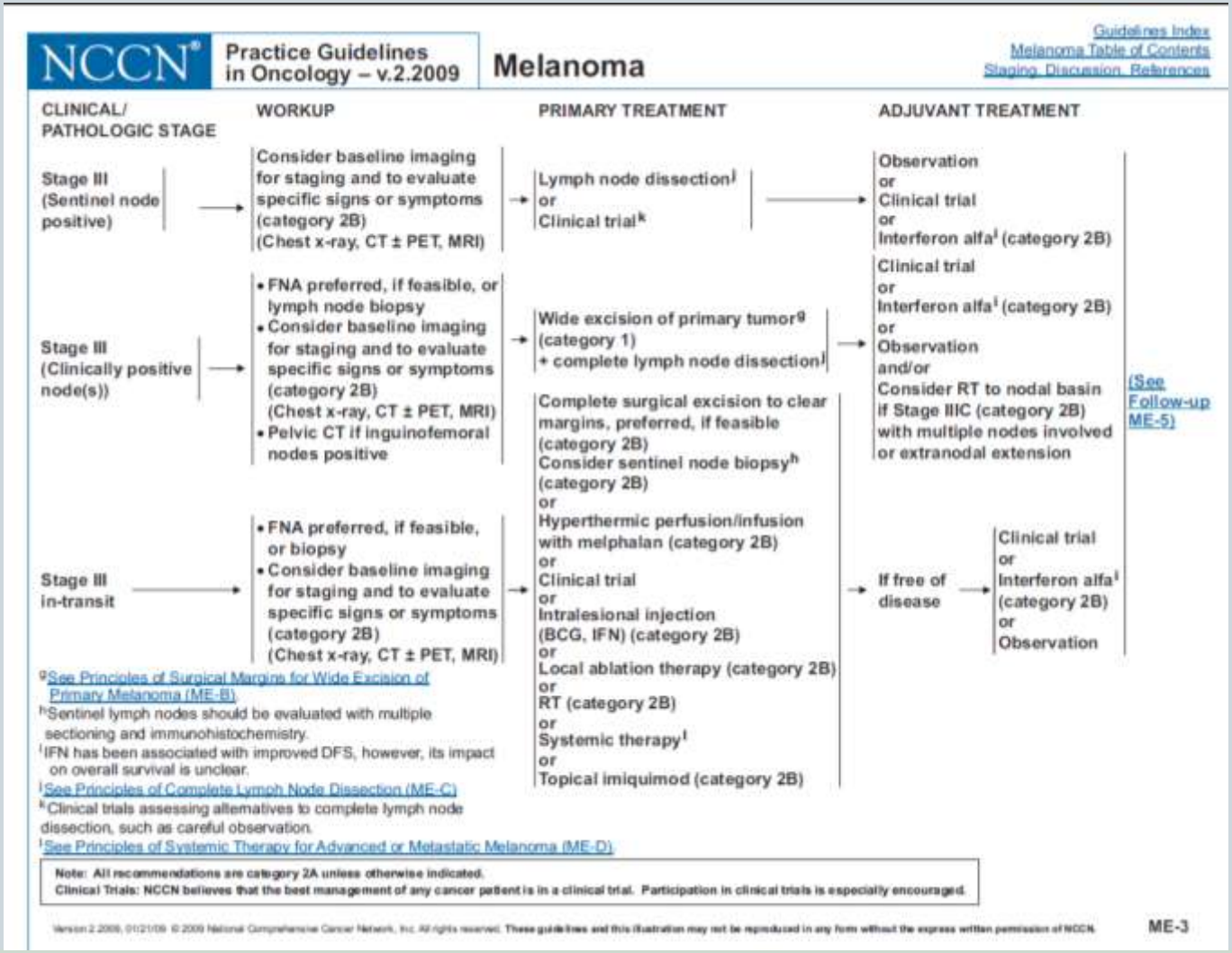
A Day In The Life…

Of a Medical Oncologist and Sarah

Sarah S.

- 37-year-old nurse, red-haired, Irish
- Tumor characteristics
  - 3mm ulcerated primary on posterior right arm
  - Single positive sentinel lymph node
  - 0/10 nodes positive on axillary dissection
- Stage IIIB melanoma
  - 47% risk of death at 5 years
  - Standard regimen: 1 month high-dose interferon, 11 months moderate dose; lowers risk of relapse ~10% with unclear impact on survival
  - Associated symptoms: fatigue, mood disturbance, autoimmune dysfunction
- Patient concerns
  - Family history: Mother died from melanoma
  - Infertility

Adjuvant interferon for Sarah S?



NCCN® Practice Guidelines in Oncology – v.2.2009

Melanoma

Guidelines Index
Melanoma Table of Contents
Staging, Discussion, References

CLINICAL/ PATHOLOGIC STAGE	WORKUP	PRIMARY TREATMENT	ADJUVANT TREATMENT
Stage III (Sentinel node positive)	Consider baseline imaging for staging and to evaluate specific signs or symptoms (category 2B) (Chest x-ray, CT ± PET, MRI)	Lymph node dissection[j] or Clinical trial[k]	Observation or Clinical trial or Interferon alfa[l] (category 2B)
Stage III (Clinically positive node(s))	• FNA preferred, if feasible, or lymph node biopsy • Consider baseline imaging for staging and to evaluate specific signs or symptoms (category 2B) (Chest x-ray, CT ± PET, MRI) • Pelvic CT if inguinofemoral nodes positive	Wide excision of primary tumor[g] (category 1) + complete lymph node dissection[j]	Clinical trial or Interferon alfa[l] (category 2B) or Observation and/or Consider RT to nodal basin if Stage IIIC (category 2B) with multiple nodes involved or extranodal extension
Stage III in-transit	• FNA preferred, if feasible, or biopsy • Consider baseline imaging for staging and to evaluate specific signs or symptoms (category 2B) (Chest x-ray, CT ± PET, MRI)	Complete surgical excision to clear margins, preferred, if feasible (category 2B) Consider sentinel node biopsy[h] (category 2B) or Hyperthermic perfusion/infusion with melphalan (category 2B) or Clinical trial or Intralesional injection (BCG, IFN) (category 2B) or Local ablation therapy (category 2B) or RT (category 2B) or Systemic therapy[l] or Topical imiquimod (category 2B)	If free of disease → Clinical trial or Interferon alfa[l] (category 2B) or Observation

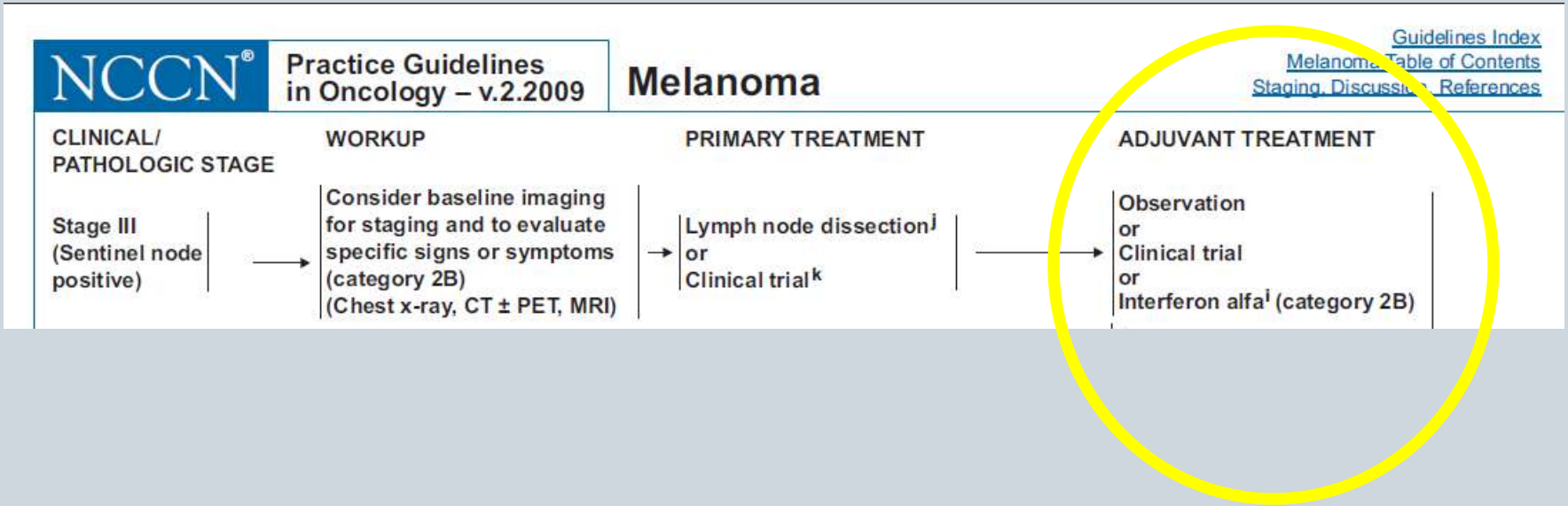
(See Follow-up ME-5)

[g] See Principles of Surgical Margins for Wide Excision of Primary Melanoma (ME-B).
[h] Sentinel lymph nodes should be evaluated with multiple sectioning and immunohistochemistry.
[l] IFN has been associated with improved DFS, however, its impact on overall survival is unclear.
[j] See Principles of Complete Lymph Node Dissection (ME-C)
[k] Clinical trials assessing alternatives to complete lymph node dissection, such as careful observation.
[l] See Principles of Systemic Therapy for Advanced or Metastatic Melanoma (ME-D)

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

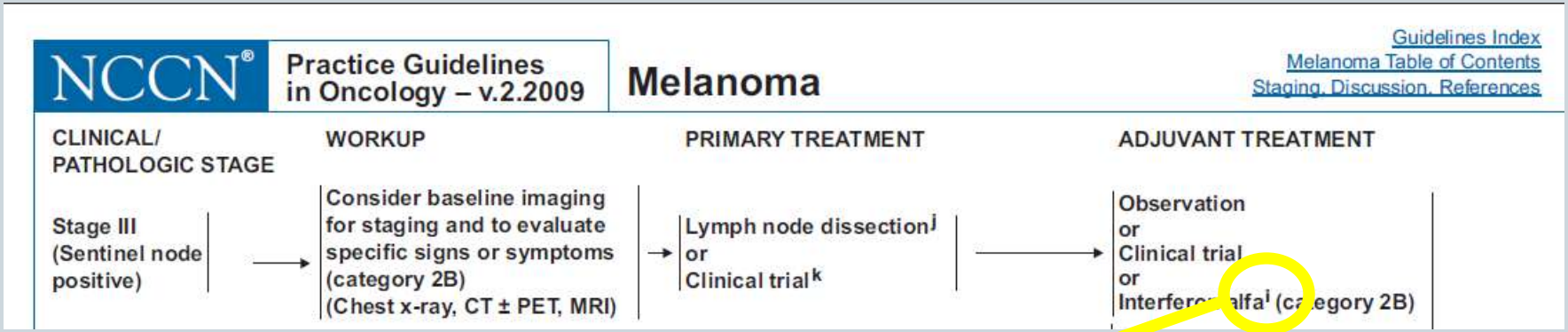
ME-3

Adjuvant interferon for Sarah S?



Observation vs Clinical Trial vs Interferon

Adjuvant interferon for Sarah S?



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i. IFN has been associated with improved DFS, however, its impact on overall survival is unclear

Relapse free and overall survival with high dose adjuvant interferon

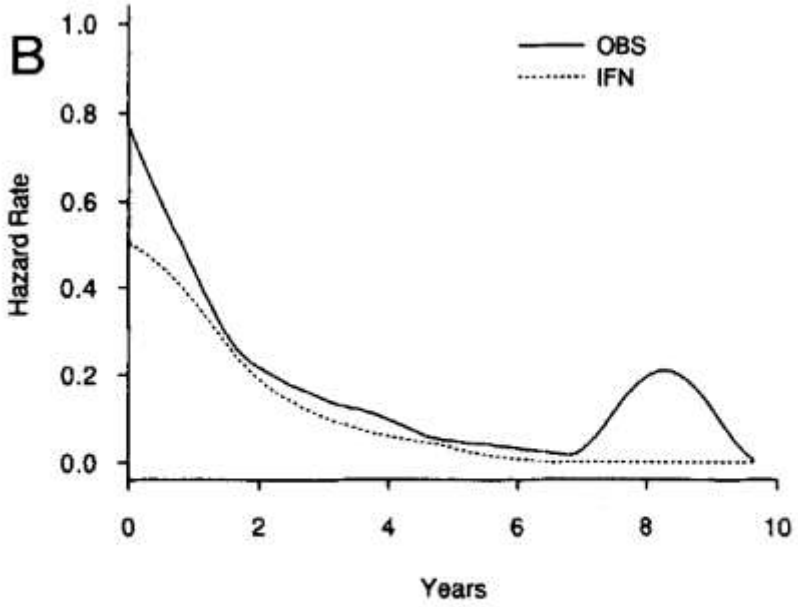


Fig 2. Relapse-free survival of eligible patients (A) and estimated hazard of relapse over time for eligible patients participating in E1684 (B). OBS, observation.

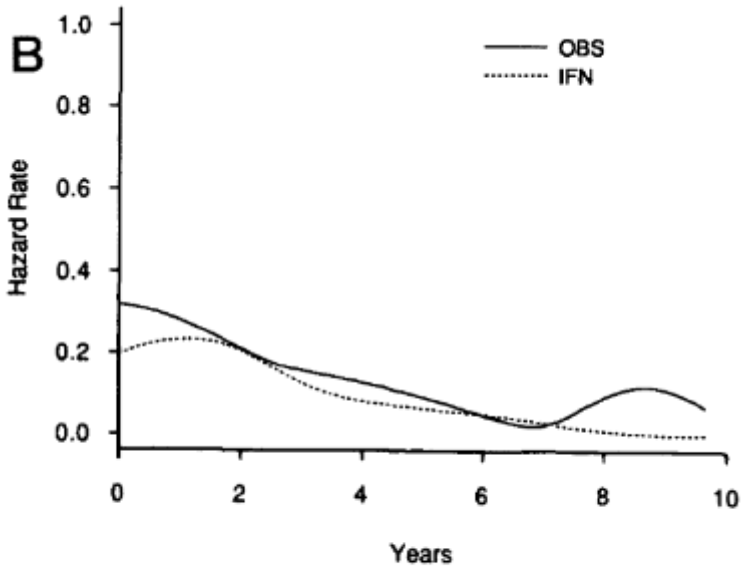


Fig 3. Overall survival of eligible patients (A) and estimated hazard of death over time for eligible patients participating in E1684 (B).

Kirkwood et al, JCO 1996 14: 7-17.

Impact of interferon on quality of life

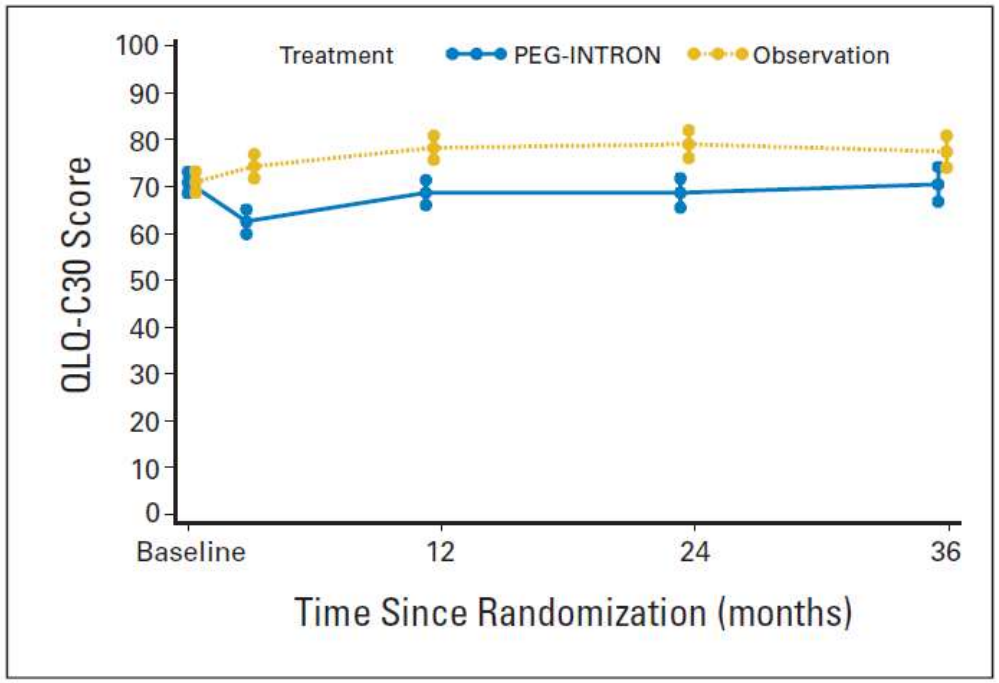


Fig 3. Primary health-related quality-of-life end point. Quality of Life Questionnaire (QLQ) -C30 scores for global health status and quality of life, measured by mean score plus 99% CI. PEG-INTRON, pegylated interferon alfa-2b.

Bottomley et al, JCO 2009 27: 2916-23.

Can we shorten the treatment period?

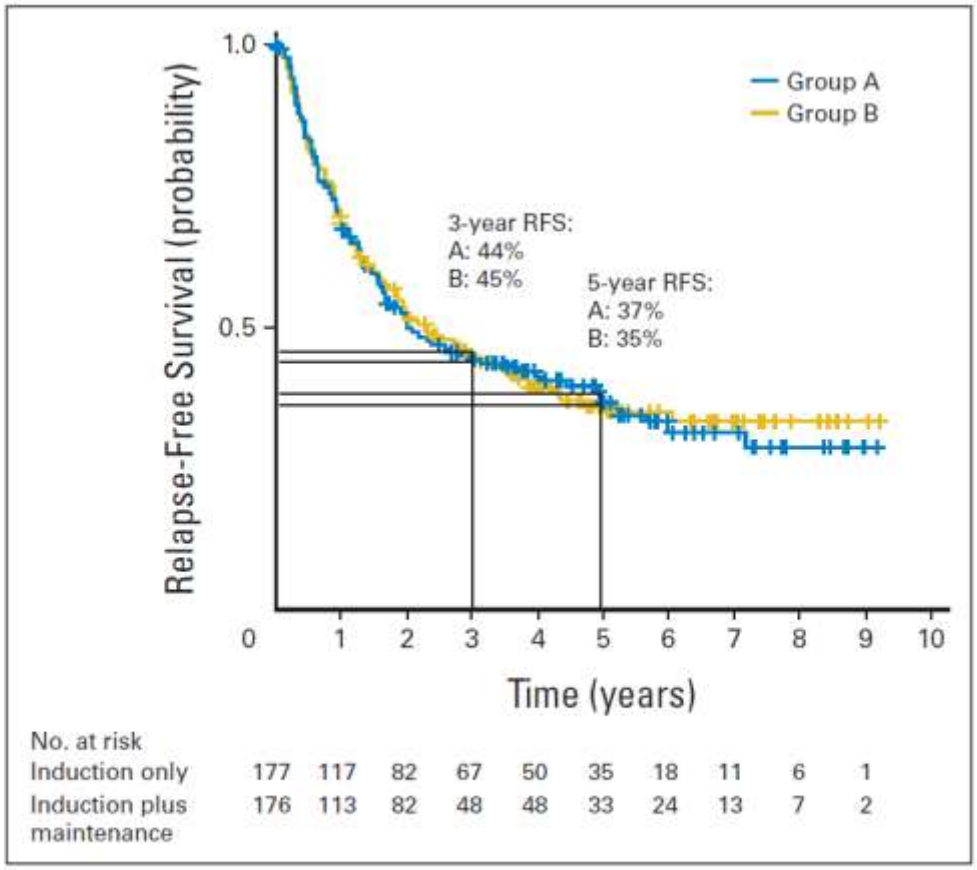
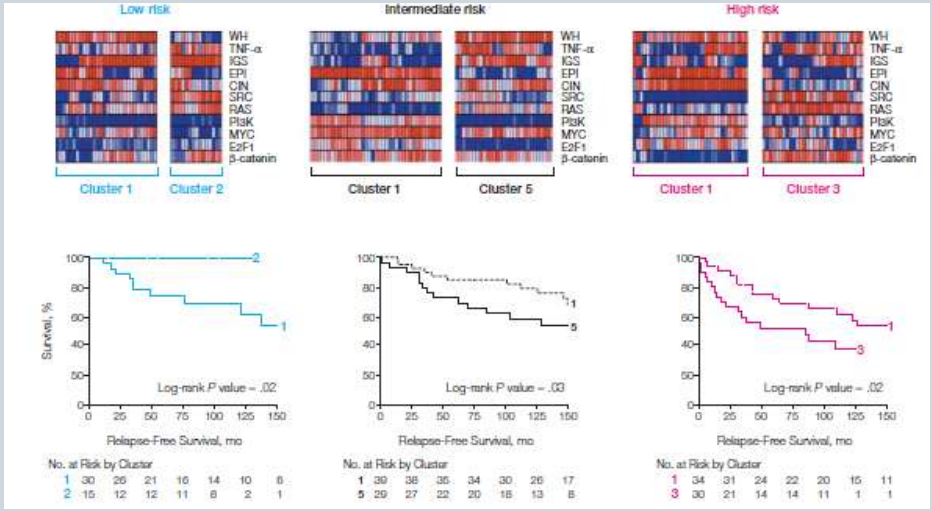


Fig 2. Kaplan-Meier curves for relapse-free survival (RFS) in the two randomization groups. Blue line, arm A; gold line, arm B.

Pectasides et al, JCO 2009 27: 939-44.

Will newer information help?

ABL
AKT1
AKT2
BRAF
CDK
CTNNB1 (b-catenin)
EGFR
ERBB2 (HER2)
FBX4
FBXW7
FGFR1
FGFR2
FGFR3
FLT3
GNAQ
HRAS
KIT
KRAS
MEK1
MET
NRAS
PDGFRA
PIK3CA
PTPN11
RET
SOS1
TP53



Molecular mutation analyses for melanoma provided by Oregon

Gene expression signatures, clinicopathological features, and individualized therapy in breast cancer. Acharya CR, et al
JAMA. 2008 Apr 2;299(13):1574-87.

Welcome to Adjuvant! Online - Microsoft Internet Explorer

File Edit View Favorites Tools Help Address https://www.adjuvantonline.com/breast

Back Search Favorites

Links CNN Interactive UCLA Google Junk.zip Mednet UCLA-PubMed Me

Search Mail IM Allowed Yellow Pages Maps Shopping Quotes

- Adjuvant! Home
- Messages
- Breast Cancer
- Colon Cancer
- Lung Cancer
- Downloads
- Online Resources
- Personal Info
- Logout
- Intended Use
- FAQs
- Contact Us

Adjuvant! Online

Decision making tools for health care professionals

Adjuvant! for Breast Cancer (Genomic Version 7.0)

Patient Information:

Present Age: 55

Comorbidity: Minor Problems

ER Status must be initially positive.

Nodal status must be node negative.

GH Recurrence Score: 10

10 Yr Risk of Metastases: 7

Planned Therapy:

Horm: Aromatase Inhibitor for 5 yrs

Chemo: 3rd Generation Regimens

Chemotherapy Effectiveness: 45

(Proportional Risk Reduction)

Resulting Graphs

Only Hormonal Therapy:

87.7 % alive and without metastases in 10 years.

6.8 % relapse. (Develop metastatic disease)

5.5 % die of causes other than breast cancer.

Hormonal Therapy and Chemotherapy:

87.7 % alive and without metastases in 10 years. Plus...

2.9 % alive and without relapse due to chemotherapy.

3.8 % relapse. (Develop metastatic disease)

5.6 % die of causes other than breast cancer.

Print PDF Online Help

Sarah S. needs a bridge

Rapid Learning Healthcare – IOM, 2007

Data that are routinely collected in patient care feed into an ever-growing databank, or set of coordinated databases.

The system learns by routinely analyzing captured information, iteratively generating evidence, and constantly implementing new insights into subsequent care.

Rapid Learning Healthcare – IOM, 2007

Reliable Data

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ng

bases.

ystem learns by routinely analyzing captured information, iteratively generating evidence, and constantly implementing new insights into subsequent care.

Rapid Learning Cancer Care at Duke

- Start off with electronic patient-reported outcomes (ePRO) data, and then build in additional linked datasets over time
- Endeavor to obtain “research-quality” clinical data
- Reliable data can be parsed out for clinical trials, clinical care, quality monitoring, and CER simultaneously

(Abernethy et al, *Health Services Research,* 2008)

Duke Rapid Learning Cancer Clinics

New datasets can be sequentially added, starting at the patient level, using warehousing or federated models. The key element is patient-level linkage.

ePRO data

Clinical and administrative data

Clinical trials and research related data

Molecular and biological data

DukeMedicine

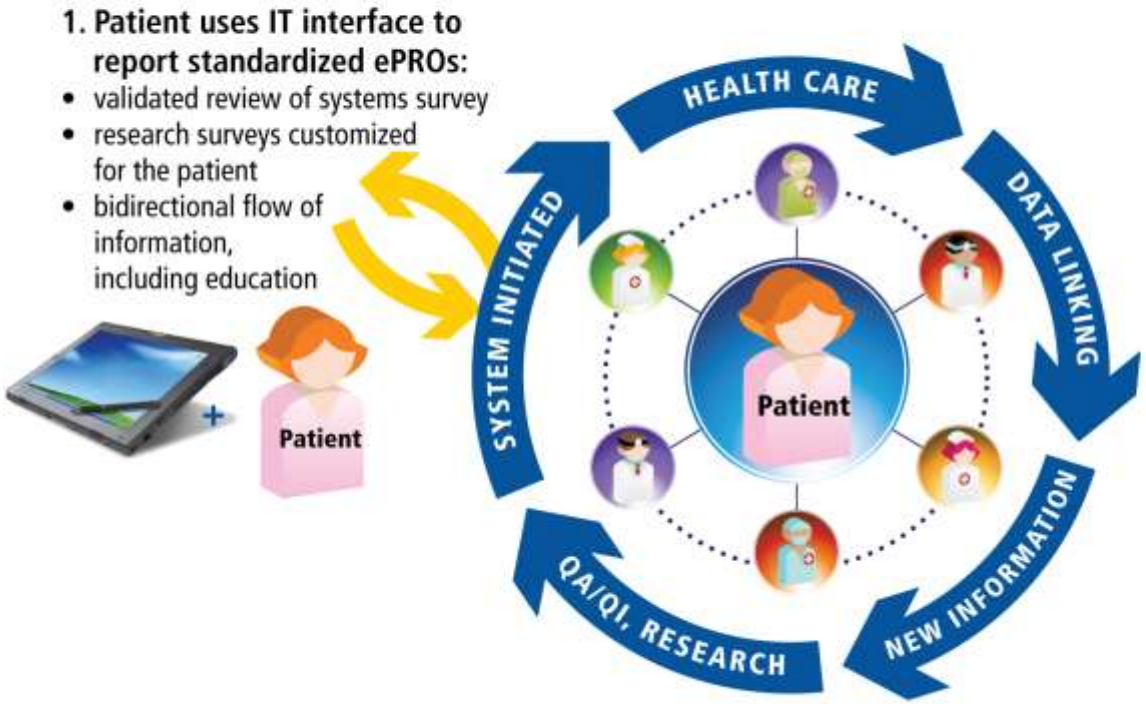
Patient-centered rapid learning cancer care

Data analysis and CER

Implement new evidence

Assess impact of implementation of new evidence and refine Interventions; recurrent CER

Rapid Learning Cancer Care



Rapid Learning Cancer Care

2. Patient-level ePRO data used for:
- longitudinal reporting at point of care
- distribution to clinical investigators
- clinical annotation for biospecimens

1. Patient uses IT interface to report standardized ePROs:
- validated review of systems survey
- research surveys customized for the patient
- bidirectional flow of information, including education

Rapid Learning Cancer Care

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3. Data drive improvement in patient care:

- ePRO data
- Laboratory, clinical, imaging, pathology, social and other information
- Data inform disease management, symptom management and supportive care

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4. Data sets are linked
- Clinical, ePRO, registry, administrative, clinical trials, basic sciences and other datasets
- Linkage at the individual patient level using warehousing and federated approaches
- Data security and confidentiality
- Data governance and use policies

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5. Aggregated data used for:
- QA/QI
- CER
- new research directions

Rapid Learning Cancer Care

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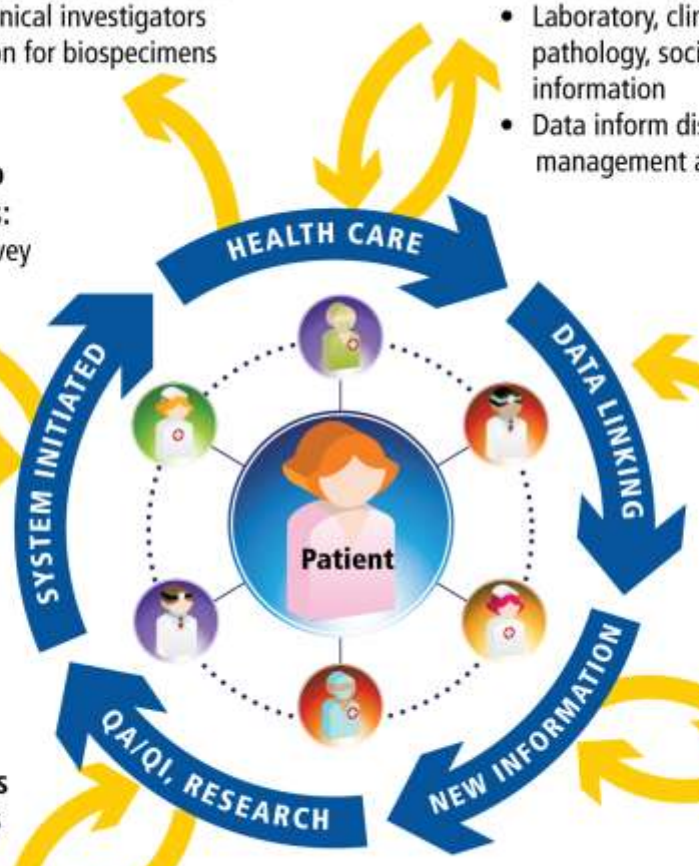

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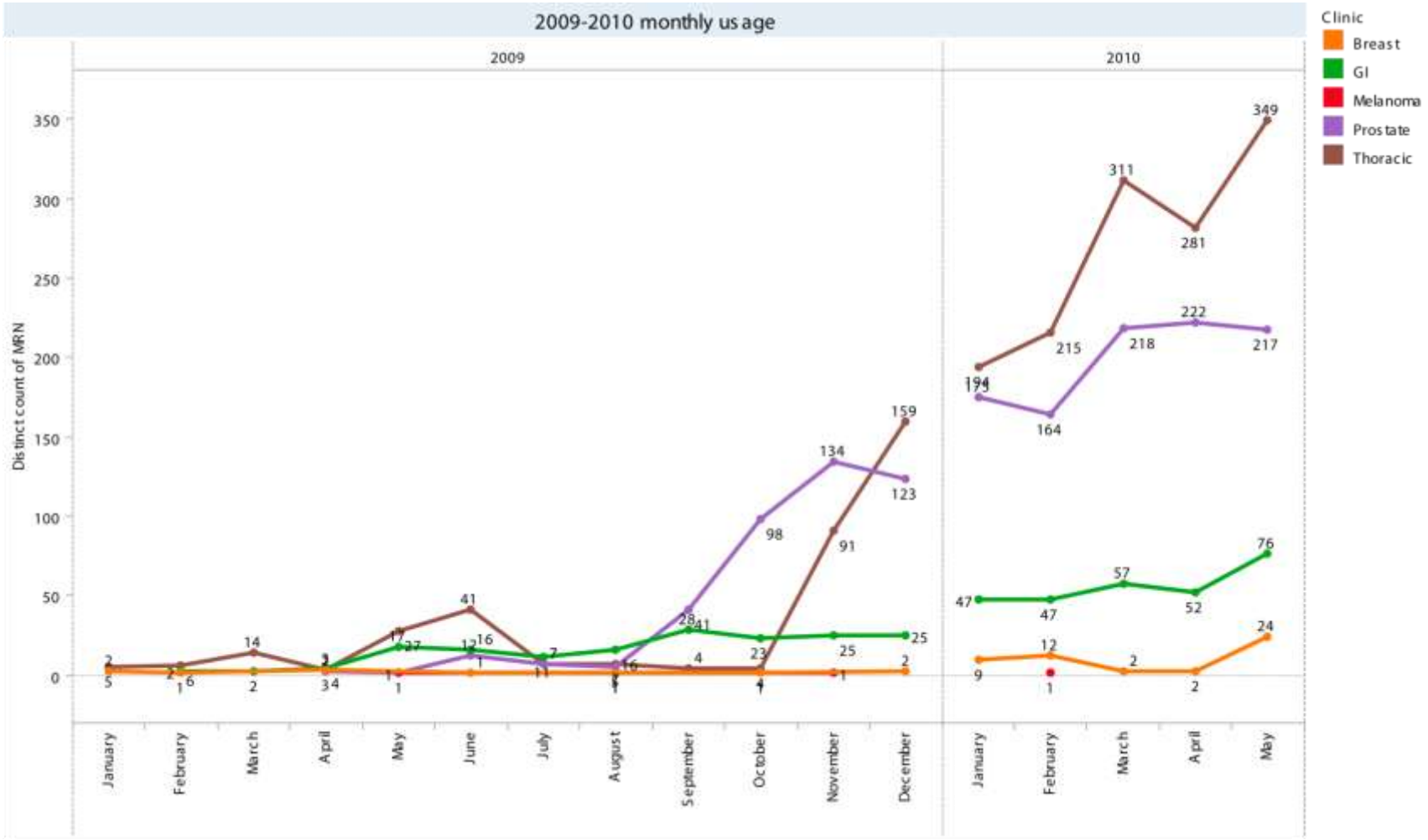
- new research directions

6. Data simultaneously drive quality and research initatives
- New information and evidence is generated through continuous data analysis
- New evidence is returned to the clinic through systematic implementation and evaluation

e/Tablet use in Duke Oncology by clinic



	Breast	GI	Lung	Total N
	N (%)	N (%)	N (%)	N (%)
Total N	65 (100)	113 (100)	97 (100)	275 (100)
Nausea (queasy feeling)				
0: none	21 (32)	43 (38)	38 (39)	102 (37)
1-3: mild	21 (32)	31 (27)	38 (39)	90 (33)
4-6: moderate	12 (18)	23 (20)	17 (18)	52 (19)
7-10: severe	11 (17)	16 (14)	4 (4)	31 (11)
Vomiting				
0: none	51 (78)	73 (65)	72 (74)	196 (71)
1-3: mild	6 (9)	24 (21)	20 (21)	50 (18)
4-6: moderate	4 (6)	9 (8)	2 (2)	15 (5)
7-10: severe	4 (6)	7 (6)	3 (3)	14 (5)
Constipation				
0: none	22 (34)	53 (47)	39 (40)	114 (41)
1-3: mild	19 (29)	25 (22)	34 (35)	78 (28)
4-6: moderate	14 (22)	27 (24)	18 (19)	59 (21)
7-10: severe	10 (15)	8 (7)	6 (6)	24 (9)
Diarrhea				
0: none	31 (48)	40 (35)	55 (57)	126 (46)
1-3: mild	20 (31)	39 (35)	31 (32)	90 (33)
4-6: moderate	11 (17)	27 (24)	7 (7)	45 (16)
7-10: severe	3 (5)	7 (6)	4 (4)	14 (5)

Sexual distress

- >30% breast, GI, and lung cancer patients with moderate to severe
- Correlated with QOL, functional status, symptoms
- Oncologists typically sidestep the issue
- Reorganize education and patient care
- Developed flexible coping model
- ACS funded randomized trial
- Reinvestment of lessons learned

7 Pillars of Personal Recovery Highlighted in the Pathfinders Program

The Seven Pillars of Personal Recovery

hope	balance	inner strengths	self care	support	spirit	life review
"I am rediscovering hope in my life"	*"I am taking my life back from cancer."*	*"I understand the power within me."*	*"I am doing all I can to help myself be well."*	*"I am giving and receiving the support I need."*	*"I am exploring my beliefs about life, death and Spirit."*	*"I am fully present in the journey of my life."*

Pathfinders intervention timeline

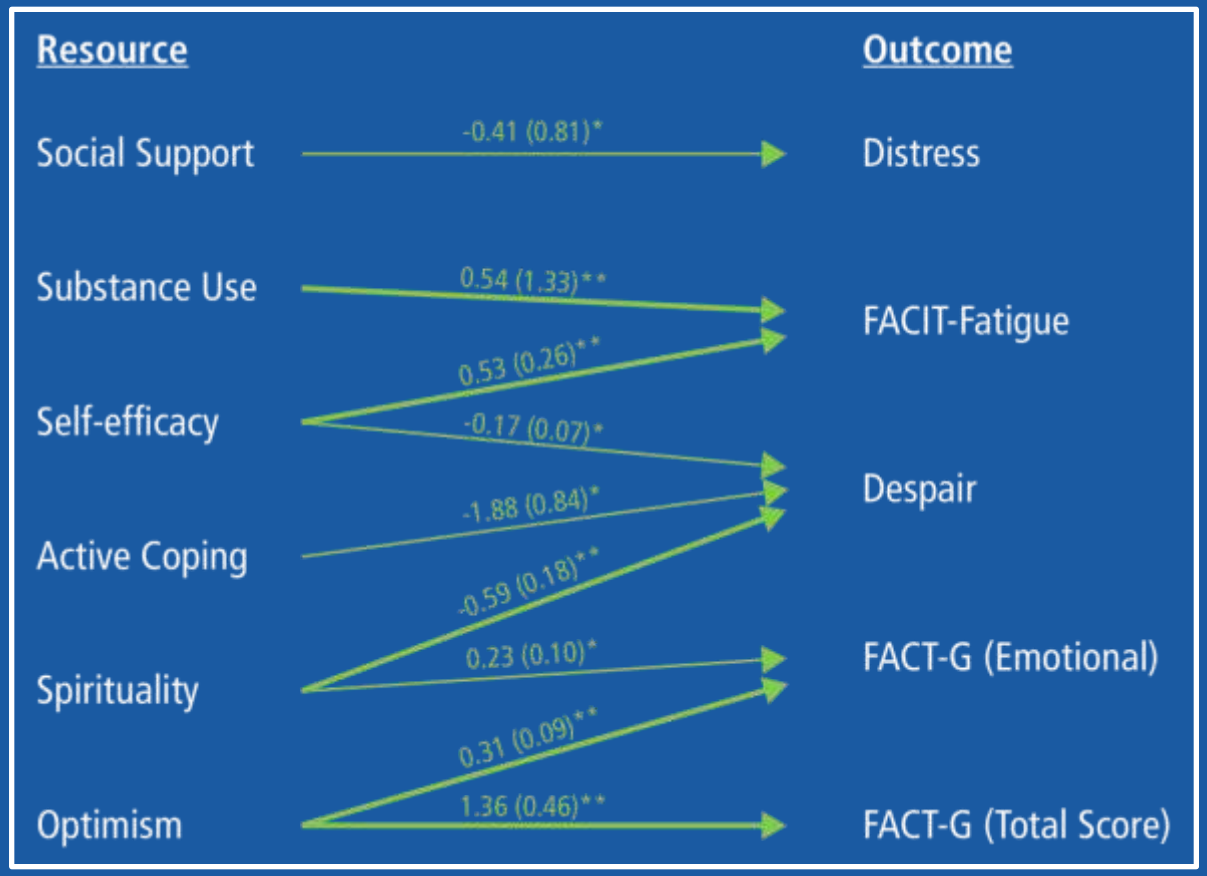
DukeMedicine

Duke Cancer Care Research Program

Patient Care Monitor (PCM) Subscales

Scale/Subscale	N (3 & 6 mo)	Baseline Mean (SE)	3 Month Change from Baseline Mean (SE)	6 Month Change from Baseline Mean (SE)	Implica-tions of results
General Physical Symptoms	36 28	26.23 (2.59)	-3.58 (1.84) P=0.0600	-3.85 (2.48) P=0.1322	**better**
Treatment Side Effects	36 28	12.5 (1.36)	-0.92 (1.52) P=0.5472	-1.89 (1.75) P=0.2903	**better**
Distress	36 28	11.36 (1.82)	**-3.42 (1.21)** **P=0.0078**	**-4.11 (1.17)** **P=0.0015**	**better**
Despair	36 28	11.53 (2.68)	**-4.53 (1.56)** **P=0.0062**	**-6.91 (2.71)** **P=0.0163**	**better**
Impaired Performance Status	30 25	12.73 (2.17)	-1.03 (1.61) P=0.5249	0.48 (1.82) P=0.7942	no change
Impaired Ambulation	35 27	4.49 (1.11)	-1.31 (0.84) P=0.1278	0.07 (1.13) P=0.9481	no change
Quality of Life	30 25	-13.52 (1.85)	**2.88 (0.97)** **P=0.0058**	**2.66 (1.45)** **P=0.0786**	**better**

Independent Associations between Resources and Quality of Life Outcomes



NOTE: All models adjusted for baseline outcome score, age, education, performance status; Numeric values represent parameter estimates (standard errors). Abbreviations: FACT-G, Functional Assessment of Cancer Therapy – General Version; FACIT, Functional Assessment of Chronic Illness Therapy.

* P<0.05; ** P<0.01

ePRO system to triage in the clinic for psychosocial distress

- Levels of psychosocial distress
- Train all clinic staff
- Triage to different services based upon ePRO report
  - Distress T score <50 – no intervention
  - Distress T score 51-55 – education resource center
  - Distress T score 56-60 – Cancer Patient Support Program
  - Distress T score 61-65 – Pathfinders
  - Distress T score >65 – Psychology/psychiatry

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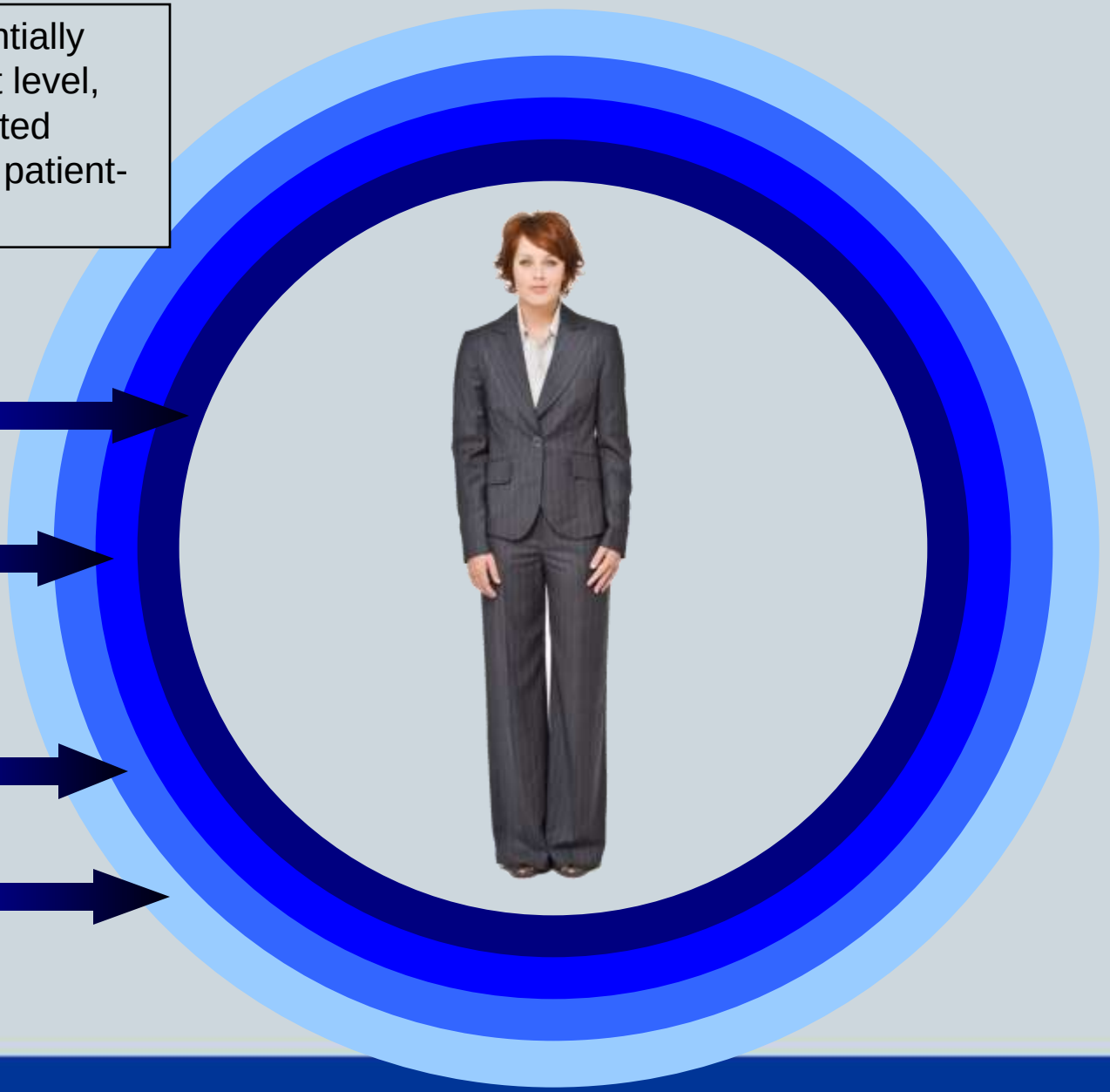
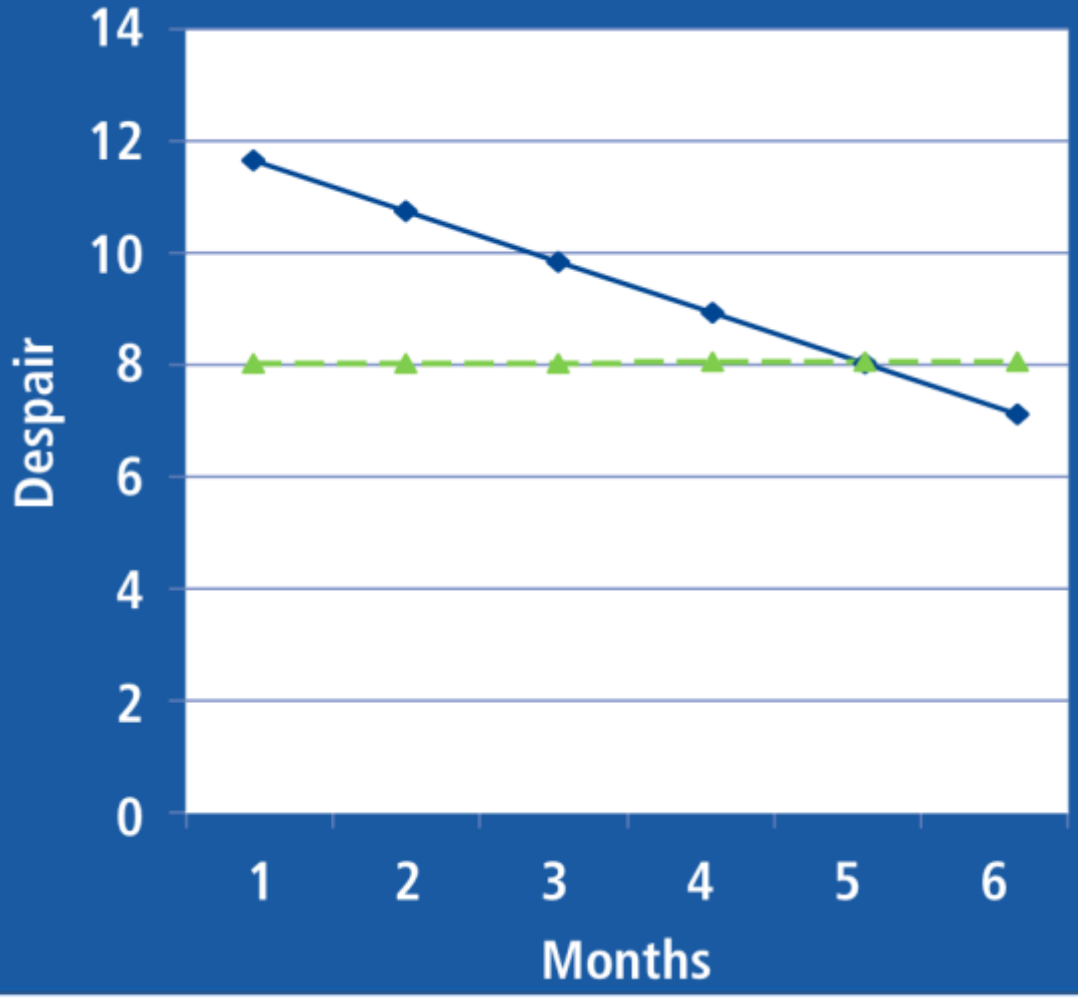


Estimated trajectories of despair scores over time



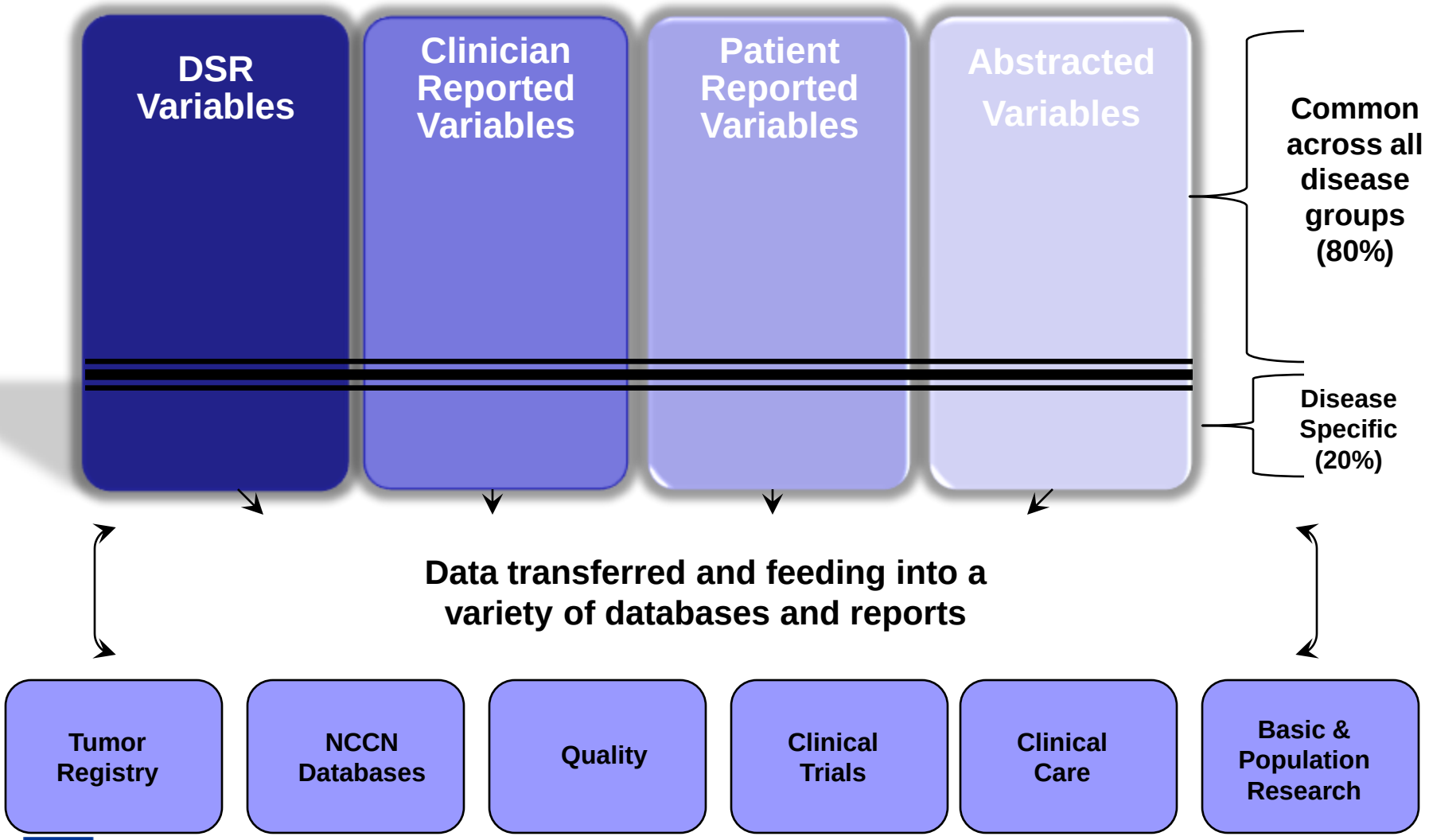
high vs. low (i.e., one SD above the mean vs. one SD below the mean) average payment per month of survival

Lower payments
Higher payments

DukeMedicine

Duke Cancer Care Research Program

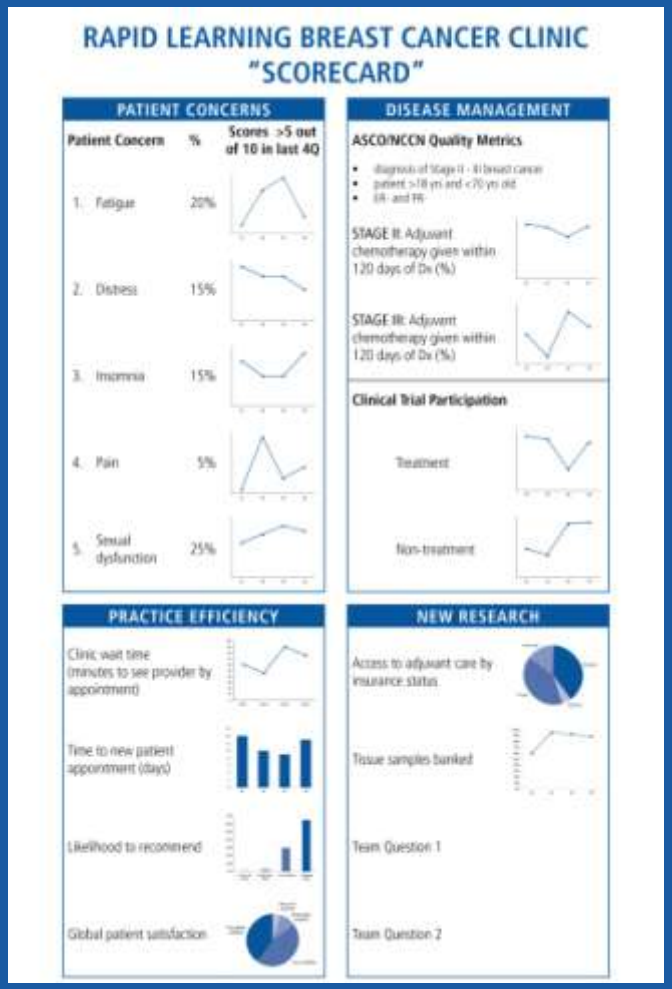
Oncology Data Mart



DukeMedicine

Moving forward

- Embedding randomization
- Visualization
- Rapid cycle learning
- Rapid learning cancer clinic scorecards that include ePROs as a core component of the model
- Transfer lessons learned to disease treatment



Rapid Learning Healthcare – IOM, 2007

Reliable Data

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bases.

ystem learns by routinely analyzing captured information, iteratively generating evidence, and constantly implementing new insights into subsequent care.

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RTW